Grantsmanship and Funding

Imaging New Investigator Perspective
Sarah McGuire, Ph.D.
University of Iowa

2013 AAPM

Funded Proposal

- Improve outcomes for pelvic cancer patients by reducing acute and chronic hematologic toxicity
  - Enable patients to complete a full course of chemotherapy
  - Potential for dose escalation or new combinations of chemoradiation therapies
- Use a non-invasive molecular imaging tool to predict bone marrow toxicity

Funded Proposal

- Central Hypothesis: FLT PET imaging for radiation therapy planning and response assessment can improve outcome for pelvic cancer patients by reducing both short and long term hematologic toxicity.

Funded Proposal

- Specific Aims:
  1. Determine the effect of patient-specific bone marrow spatial maps measured with FLT PET on the ability to spare proliferating bone marrow using IMRT planning for pelvic radiation therapy.
  2. Use FLT uptake change in pelvic bone marrow during and after therapy as a biomarker to establish the relationship between radiation dose and both acute grade 2 or higher and long term systemic toxicities.

FLT

- A fluorinated thymidine analog, 3'-deoxy-3'-[18F] fluorothymidine (FLT) incorporated into DNA synthesis
- Promising PET tracer for evaluating tumor-proliferation and bone marrow activity
- Less prone to false positives due to inflammation or changes in metabolism than FDG
- Shows response early in RT for both tumor and normal tissues

Funded Proposal

- Study Outline
  - Enroll 24 subjects receiving chemoRT for pelvic cancer
  - Acquire 5 FLT PET images
    - 1 Simulation scan to identify active bone marrow
    - 2 on treatment scans (after 1 and 2 weeks of chemoRT) to monitor acute bone marrow radiation response
    - 2 post treatment scans (30 days and 1 year after therapy) to monitor chronic bone marrow radiaiton response

Funded Proposal

- Data endpoints
  - Change in FLT uptake in pelvic bone marrow during and after therapy from simulation
  - Change in CBCs during and after therapy from simulation
  - Spatial FLT PET pelvic bone marrow maps
  - Radiation dose to bone marrow volume tolerances to limit systemic toxicity

Assemble a Good Team

- Buy in from leadership
  - Radiation Oncology Department Chair created translational research environment
  - Medical Physics Director fostered collaborations and ideas
- Support Staff
  - Dedicated people to support the grant and clinical trial process
  - Clinical trial nurses keep the machine running

Use Available Resources

- Novel nuclear medicine imaging technique applied in a new way
  - FLT is not available many places in the US
  - FLT provides different biological information
  - Use principles developed for H&N tumor imaging at our institutions to a new site
  - Apply biological imaging to normal tissues instead of tumor tissues
- RadOnc has a PET/CT

Manage (a lot of) Failure

- Seed grants applications were rejected
  - Scope was too large
  - Can't have a result in a short enough time frame
- R21 application was scored but not funded
  - Concept was not clear
  - May have had similar issues to seed grants: too much in two small a time frame (2 yrs)
  - Reapplications occurred right at the transition from 3 resubmissions to 2

Institutional Support

- Attempts to get funding for preliminary data failed
- Director of the Nuclear Medicine Dept. believed in the project and found funds for initial subjects
- Radiation Oncology Dept. supported the project and provided scanner time and worked with NucMed to design workflow

Use Feedback

- Failed applications helped illustrate how to communicate the study more effectively
- Departmental personnel helped determine a functional workflow
- Subjects helped determine what patients would be willing to tolerate
- Data helped determine what time points were extraneous or missing

Simplify

- Initially wanted to image tumor and bone marrow in same subjects with both static and dynamic PET imaging
- Difficult to combine a therapy response with a normal tissue response
- Normal tissue response offered more flexibility
- Dynamic imaging was too time consuming and did not provide much value

Broaden Scope

- Initially focused on one patient population
  - R21 feedback expressed concern about lack of significance because of smaller patient pool
  - Accrual was more difficult with smaller patient pool
- Normal tissue focus allowed for more tumor types in the pelvis
- More tumor types tests hypothesis in more situations

Get Outside Input

- Publications
  - 4 abstracts at 4 meetings within a year before submitting R01 from preliminary data
  - 2 manuscripts from H&N data used to show proof of concept
- Talked to experts in the field
  - At national meeting
  - Invited to my Institution

Write and Rewrite

- Each application was a modification of the one before
- Probably ~4 years in total
- Had multiple people read it and reread it
- Worked to be as clear as possible, but can still be blinded by your own bias

Outliers

- Luck is probably a factor
  - Right people in the right place at the right time
  - Right tool available
  - Right environment for a clinical study
- Perseverance is probably also a factor
  - Learn from failure and try again
  - Have a backup plan
  - Keep big picture focus